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# Chiroptical Properties, Structure, and Absolute Configuration of Heterosubstituted 2(*5H*)-Furanones

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*ABSTRACT* Chiroptical properties of a series of 3 and/or 4-heterosubstituted 2(*5H*)-furanones were investigated with respect to correlation with absolute configuration. The n − π* and π − π* Cotton effects have been assigned on the basis of comparison with the UV spectra in solvents of varying polarity. It is demonstrated that the n − π* transition in 4-amino substituted 2(*5H*)-furanones appears at shorter wavelength with respect to the π − π* transition. With the exception of 4-pyrrolidino and 4-benzylamino substituted 2(*5H*)-furanones, other heterosubstituted 2(*5H*)-furanones follow the butenolide configurational rule (Gawronski et al. J. Org. Chem. 61:1513–1515, 1996). Absolute configuration of 2(*5H*)-furanone derivatives can also be assigned according to the sign of the Cotton effect (of unknown origin) at 200–230 nm. The structure of four representative sulfur and nitrogen substituted 2(*5H*)-furanones has been analyzed by X-ray diffraction. The results indicate planarity of the furanone ring and extended conjugation in 4-amino substituted 2(*5H*)-furanones. *Chirality 9:537–544, 1997.* 

*KEY WORDS:* Circular dichroism; helicity rule; X-ray structure determination; ultraviolet spectra; n − π* and π − π* bands

Chiral 2(*5H*)-furanones of general formula **A** have recently emerged as important synthetic intermediates.[1] Since these compounds are available from achiral substrates via several asymmetric synthesis protocols,[2–6] knowledge of their absolute configuration is of primary importance. Recently we have demonstrated that absolute configuration of furanones **A** can be readily and unequivocally determined from the CD spectrum. The relationship between the absolute configuration at C(5) of a furanone moiety and the sign of the n − π* and π − π* Cotton effect is shown in Figure 1.[7]

The validity of the helicity rule shown below has been demonstrated for 2(*5H*)-furanones having $\mathbf{R}^1$, $\mathbf{R}^2$ = hydrogen or alkyl substituents. In recent years, chiral 2(*5H*)-furanones with heterosubstituents in positions 3 and 4 have been synthesized in several laboratories.[8–11] In view of their potential applications in asymmetric synthesis it was of interest to determine the applicability of the configurational rule for 2(*5H*)-furanones[7] to the derivatives **B** substituted with heteroatoms at C(3) and C(4). One immediate concern was to correctly assign the n − π* and π − π* transition Cotton effects in derivatives **B,** in view of the expected large shifts of the absorption maxima due to the substitution and solvent effects.

Here we present the results of our CD/UV study of a series of optically active 2(*5H*)-furanones **1–31** of known absolute configuration, synthesized in these laboratories.

## RESULTS AND DISCUSSION

### *Assignment and Positions of the CD Bands*

Unsubstituted butenolide chromophore (**A,** $R^2$, $R^3$ = H) shows $UV_{max}$ at 201 nm ($\epsilon$ $10^4$) in methanol. This band is due to the π − π* transition of the α,β-unsaturated carbonyl chromophore. The corresponding n − π* transition has low intensity in the UV spectrum but can be readily detected in the CD spectrum as a Cotton effect at ca. 240 nm.[7] As expected for the transitions involving polar carbonyl group, donor type substituents attached to the conjugated C=C bond bring about large batochromic shift of the π − π* transition absorption maximum. This can be readily seen in the UV data for 2(*5H*)-furanones collected in Tables 1–5.

The position of the $UV_{max}$ ranges from 220 nm in C(4)-bromo substituted 2(*5H*)-furanone to 265 nm in C(4)-amino substituted 2(*5H*)-furanones in n-heptane solution. Typically for the π − π* band, its position is red-shifted in polar methanol solution, 5–8 nm for C(4)-mercapto and 8–9

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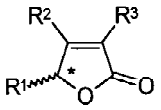
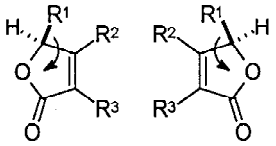


**A, B**

**A** $R^1$ = alkyl, alkoxy; $R^2$, $R^3$ = H, alkyl

**B** $R^1$ = alkyl, alkoxy; $R^2$ and/or $R^3$ = Br, Cl, OR, SR, $NR_2$



| $R^1$-C-C=C helicity | P | M |
|---|---|---|
| n-π* Cotton effect | − | + |
| π-π* Cotton effect | + | − |

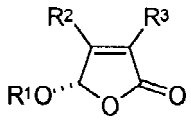
**Fig. 1.** 2(*5H*)-Furanone configurational rule.

nm for C(4)-amino substituent. The intensity of the π − π* transition absorption band increases with the donor character of C(4) substituent: the (secondary or tertiary) amino group brings about two-fold increase of $\epsilon_{max}$. Also typically for the π − π* transition of the charge-transfer type, the intensity of the band increases in polar methanol solution compared to nonpolar heptane solution.

The CD spectra of the heterosubstituted 2(*5H*)-furanones **B** are more complicated compared to 2(*5H*)-furanones of type **A.** At least three Cotton effects are observed in the majority of cases and assignment of the CD bands becomes of primary importance for the interpretation of the CD results in terms of the 2(*5H*)-furanone configurational rule.

The assignments of the CD bands is based on the following three features: 1) correlation of the position of the π − π* Cotton effect with the position of the corresponding π − π* transition UV band; 2) the presence of the vibrational bands in the n − π* Cotton effect in heptane solution; and 3) solvent polarity effect on the position of the CD maxima (expected red shift of the π − π* Cotton effect, blue shift of the n − π* Cotton effect).

Examples of the CD and UV spectra of differently substituted 2(*5H*)-furanones in heptane solution are presented in Figure 2. The dichloro derivative **1** features a positive n − π* Cotton effect at longer wavelength and a negative π − π* Cotton effect at shorter wavelength. The former is distinguished by its fine structure and the position of the latter (232 nm) roughly corresponds to the position of $UV_{max}$ (224 nm). In the case of 4-ethylthio substituted 2(*5H*)-furanone **7** the $UV_{max}$ at 282 nm falls in between the two



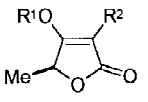
**1 -22**

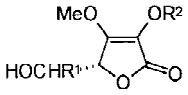
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **1** | (-)-menthyl | Cl | Cl |
| **2** | (-)-bornyl | Cl | Cl |
| **3** | (-)-menthyl | Br | H |
| **4** | (-)-menthyl | Br | Br |
| **5** | (-)-bornyl | Br | Br |
| **6** | (-)-menthyl | EtS | H |
| **7** | (-)-bornyl | EtS | Br |
| **8** | (-)-menthyl | n-$C_5H_{11}$ | Br |
| **9** | (-)-bornyl | BnS | Cl |
| **10** | (-)-menthyl | BnS | Br |
| **11** | (+)-menthyl | PhS | H |
| **12** | (-)-menthyl | PhS | Cl |
| **13** | (-)-menthyl | PhS | Br |
| **14** | (-)-menthyl |  | H |
| **15** | (-)-menthyl |  | Cl |
| **16** | (-)-bornyl |  | Cl |
| **17** | (-)-menthyl |  | H |
| **18** | (-)-menthyl |  | Cl |
| **19** | (-)-menthyl | $Et_2N$ | H |
| **20** | (-)-menthyl | BnHN | Cl |
| **21** | (-)-bornyl | BnHN | Cl |
| **22** | (-)-bornyl | BnHN | Br |

**23** R = Me

**24** R = $CH_2CH{=}CH_2$

**25** R = COOMe





**26 - 28**

**29 - 31**

**26** $R^1$ = H, $R^2$ = H

**27** $R^1$ = Me, $R^2$ = H

**28** $R^1$ = H, $R^2$ = n-Bu

**29** $R^1$ = $CH_2OH$, $R^2$ = H (L-*threo*)

**30** $R^1$ = $CH_2OH$, $R^2$ = Me (L-*threo*)

**31** $R^1$ = H, $R^2$ = Me

**Formula 1.**

CD maxima. Closer inspection of the CD curve reveals that the positive band at 305 nm belongs to the n − π* Cotton effect which overlaps with the negative π − π* Cotton effect. In methanol solution (Table 2) the n − π* Cotton effect cannot be observed as the result of additional red shift of the π − π* CD band and lack of the vibronic fine structure.

The case of 4-phenylthio substituted 2(*5H*)-furanone **12** is even more complicated. The negative CD band at 299 nm belongs to the π − π* transition with $UV_{max}$ at 281 nm (Fig. 2). The n − π* Cotton effect is seen as an irregular hump on the short wavelength slope of the CD π − π* band. The n − π* Cotton effect is positive, from the shape of the CD curve. Also there are two additional Cotton effects at 256 nm and at 212 nm (Fig. 2 and Table 2) which have the

**TABLE 1. CD and UV data of halogen substituted 2(*5H*)-furanones**

| Compound | Solvent[a] | CD, Δε (nm) n-π* (I) | CD, Δε (nm) π-π* (II) | CD, Δε (nm) III | UV, ε (nm) π-π* |
|---|---|---|---|---|---|
| **1** | M | +4.4 (251) | −7.9 (230) | +2.3 (209) | 9100 (226) |
| | H | +3.8 (252)[b] | −7.4 (232) | +1.9 (211) | 9600 (224) |
| **2** | M | +4.1 (253) | −7.2 (230) | +1.0 (208) | 9000 (226) |
| | H | +3.4 (252)[b] | −7.2 (230) | +0.5 (209) | 9500 (224) |
| **3** | M | +2.8 (252) | −4.4 (232) | +3.8 (215) | 9800 (222) |
| | H | +1.5 (257)[b] | −4.0 (230) | +2.1 (214) | 10000 (220) |
| **4** | M | +4.2 (260) | −6.3 (241) | +1.2 (212) | 9300 (241) |
| | H | +3.2 (262)[b] | −6.5 (240) | +0.5 (208) | 9400 (240) |
| **5** | M | +5.0 (259) | −7.1 (240) | +1.4 (211) | 9200 (241) |
| | H | +4.2 (262)[b] | −7.3 (240) | +1.1 (208) | 9400 (240) |

[a]M-methanol, H-heptane.
[b]Band with fine structure.

**TABLE 2. CD and UV data of 4-mercapto substituted 2(*5H*)-furanones**

| Compound | Solvent[a] | CD, Δε (nm) n-π* (I) | CD, Δε (nm) π-π* (II) | CD, Δε (nm) III | UV, ε (nm) π-π* |
|---|---|---|---|---|---|
| **6** | M | +2.9 (280) | −4.0 (248) | +10.3 (215) | 15100 (271) |
| | H | +3.9 (274)[b] | −6.9 (255)[b] | +11.3 (219) | 15200 (263) |
| **7** | M | [c] | −2.8 (291) | +6.3 (204) | 12300 (289) |
| | H | +0.6 (305)[d] | −2.6 (265)[b] | +4.3 (206) | 11400 (282) |
| **8** | M | [c] | −4.2 (295) | +6.6 (211) | 13400 (290) |
| | H | +0.4 (313)[d] | −4.2 (266)[b] | +8.3 (210) | 12200 (282) |
| **9** | M | [c] | −1.5 (297) | +5.2 (217) | 14600 (285) |
| | H | +0.2 (310)[d] | −3.1 (255)[b] | +5.4 (219) | 13300 (280) |
| **10** | M | [c] | −2.3 (299) | +4.6 (221) | 12500 (289) |
| | H | [c] | −2.9 (255)[b] | +4.2 (225) | 11000 (284) |
| **11** | M[e] | +0.7 (275) | −2.6 (245) | +6.6 (205) | 12300 (272) |
| **12** | M[f] | [c] | −6.3 (301) | +6.8 (225) | 9400 (287) |
| | H[g] | [c] | −8.2 (299) | +5.0 (227) | 9400 (281) |
| **13** | M[h] | [c] | −9.9 (303) | +6.5 (229) | 9800 (291) |
| | H[i] | [c] | −11.5 (299) | +4.9 (230) | 9500 (285) |

[a,b]see Table 1.
[c]Band not observed.
[d]n-π* band partially overlapping the π-π* band.
[e]Additional maxima: CD −1.5 (292); UV 12400 (205).
[f]Additional maxima: CD +0.3 (255), −6.2 (210); UV 5800 (251), 11900 (205).
[g]Additional maxima: CD +0.8 (256), −5.0 (212); UV 6800 sh (257), 12000 (206).
[h]Additional maxima: CD +1.1 sh (253), −6.8 (212); UV 5800 (251), 12300 (205).
[i]Additional maxima: CD +1.5 (258), −5.0 (215); UV 6100 (258), 12700 (206).

corresponding UV maxima at 257 nm and at 206 nm. These bands are due to transitions in the phenylthio chromophore and are also observed in other, structurally similar 2(*5H*)-furanones **11** and **13.**

The effect of overlapping the negative π − π* Cotton effect (II) with the positive n − π* Cotton effect (I) is also seen in the CD spectrum of 4-benzylthio substituted 2(*5H*)-furanone **9,** in methanol solution (Fig. 3).

As in the case of **12,** the n − π* transition in **9** appears at shorter wavelength, compared to the π − π* transition. This shift of bands is even more distinct in the case of 4-amino substituted 2(*5H*)-furanones. For example, 4-pyrrolidino substituted 2(*5H*)-furanone **17** displays a positive Cotton effect at 281 nm ($UV_{max}$ at 280 nm) and a negative Cotton effect at 217 nm in highly polar hexafluoroisopropanol solvent (Fig. 3). These Cotton effects are accordingly observed at 269 nm and at 249 nm in the CD spectrum measured in heptane solution.

In general, the effect of overlapping n − π* and π − π* bands is responsible in many cases for decreased intensities of the Cotton effects. This is more pronounced in polar solvents (methanol), compared to nonpolar heptane, with the exception of 4-amino substituted 2(*5H*)-furanones.

The tetronic acid derivative **26** exists as a mixture of tautomers in nonpolar solvents. In $CDCl_3$ solution the NMR spectrum shows the presence of both the enol **(26)** and the keto forms, in the ratio 3:1. The presence of the keto form in dioxane solution (ca. 30%) is evident from the NMR spectrum and from lower $\epsilon_{max}$ at 217 nm in the UV spectrum. In cyclohexane, CD spectrum reveals weak Cot-

**TABLE 3. CD and UV data of 4-amino substituted 2(*5H*)-furanones**

| Compound | Solvent[a] | CD, Δε (nm) | | | UV, ε (nm) |
|---|---|---|---|---|---|
| | | n-π* (I) | π-π* (II) | III | π-π* |
| **14** | M | +0.3 (230)[d] | −4.9 (270) | +10.4 (199) | 22600 (274) |
| | H | +0.2 (285) | −8.6 (261) | +9.0 (201) | 20200 (265) |
| | | +1.3 (232)[d] | | | |
| **15** | M | +1.1 sh (230)[d] | −5.1 (284) | +7.3 (204) | 22300 (285) |
| | H | +0.2 (305) | −7.4 (274) | +4.3 (204) | 19900 (277) |
| | | +1.5 sh (235)[d] | | | |
| **16** | M | [c] | −5.2 (283) | +5.8 (204) | 22300 (284) |
| | H | +0.3 (305)[d] | −6.4 (272) | +3.2 (204) | 19900 (276) |
| **17** | M | −2.4 (227)[d] | +4.3 (275) | +6.8 (200) | 21900 (272) |
| | H | −3.1 (249)[d] | +6.4 (269) | +4.8 (203) | 19700 (264) |
| **18** | M | −1.0 (229)[d] | +4.1 (286) | +6.1 (203) | 20000 (288) |
| | H | −1.3 (240)[d] | +4.2 (289) | +4.3 (202) | 18300 (279) |
| **19** | M | −0.8 (223)[d] | +1.0 (289) | +7.4 (199) | 20400 (273) |
| | | | −0.6 (264) | | |
| | H | −1.5 (225)[d] | +1.7 (274) | +5.4 (200) | 19300 (265) |
| | | | −1.4 (249) | | |
| **20** | M | −1.3 (229) | +2.7 (273) | +4.0 (200) | 20900 (275) |
| | H | −3.5 (234) | +5.5 (265) | +0.5 (200) | 16400 (264) |
| **21** | M | −2.7 (230) | +2.1 (275) | +5.0 (202) | 21100 (275) |
| | H | −5.6 (236) | +5.0 (269) | +1.0 (200) | 18400 (264) |
| **22** | M | −3.1 (229) | +2.0 (277) | +5.0 (203) | 20800 (277) |
| | H | −4.8 (238) | +3.6 (272) | +3.0 (205) | 18100 (267) |

[a,c,d]See Table 2.

**TABLE 4. CD and UV data of 5,5-disubstituted 2(*5H*)-furanones**

| Compound | Solvent[a] | CD, Δε (nm) | | | UV, ε (nm) |
|---|---|---|---|---|---|
| | | n-π* (I) | π-π* (II) | III | π-π* |
| **23** | M | −3.4 (231)[d] | +5.1 (274) | +13.6 (203) | 20800 (275) |
| | H | −4.6 (235)[d] | +7.2 (265) | +15.0 (202) | 18400 (264) |
| **24** | M | −2.7 (233)[d] | +2.5 (274) | +14.0 (204) | 20100 (277) |
| | H | −4.2 (238)[d] | +3.6 (267) | +15.2 (202) | 17800 (267) |
| **25** | M | −1.2 (236)[d] | +4.4 (275) | +8.5 (203) | 20300 (277) |
| | H | −2.8 (243)[d] | +3.8 (269) | +7.7 (202) | 18000 (269) |

[a,d]See Table 2.

**TABLE 5. CD and UV data of hydroxy/alkoxy substituted 2(*5H*)-furanones in methanol solution**

| Compound | CD, Δε (nm) | | UV, ε (nm) |
|---|---|---|---|
| | n-π* (I) | π-π* (II) | π-π* |
| **26** | −1.3 (231) | +1.6 (209) | 14200 (223) |
| **27** | −2.2 (227) | [c] | 13200 (219) |
| **28** | −0.5 (258) | +0.7 (230) | 9400 (230) |
| | | | 3200sh (258) |
| **29** | +1.5 (249) | −1.5 (222) | 9300 (245) |
| **30** | +1.1 (248) | −1.5 (216) | 9900 (233) |
| **31** | +1.0 (249) | −1.6 (215) | 10600 (233) |

[c]See Table 2.

ton effect, Δε +0.05 at 290 nm, due to the ketone n − π* transition. However, the keto form has very little contribution to the equilibrium in polar methanol solvent and the CD spectrum in this solvent can be treated as that of the enol form **26.**

On the basis of the UV data collected in Tables 1–5 and the discussion above, the effect of heterosubstituents at C(3) and C(4) on the absorption maximum of the α,β-unsaturated lactone is shown in Table 6.

The very large batochromic shift of the π − π* band due to the 4-mercapto or 4-amino substitution is readily recognizable. This shift, combined with the hipsochromic shift of the n − π* band, is responsible for the appearance of the n − π* Cotton effect at shorter wavelength with respect to the position of the π − π* Cotton effect in the CD spectrum of the mercapto and amino substituted 2(*5H*)-furanones (Table 7). The data of Table 7 serve as guidelines for the interpretation of the CD data (see below).

Unlike unsubstituted 2(*5H*)-furanones **A** ($R^2$, $R^3$ = H) compounds studied in this work (**1–25,** Tables 1–4) display additional short-wavelength Cotton effect at 200–230 nm in the CD spectrum. This Cotton effect (III) in many cases is the most intense one but it has no corresponding UV maximum. The position of the maximum of this CD

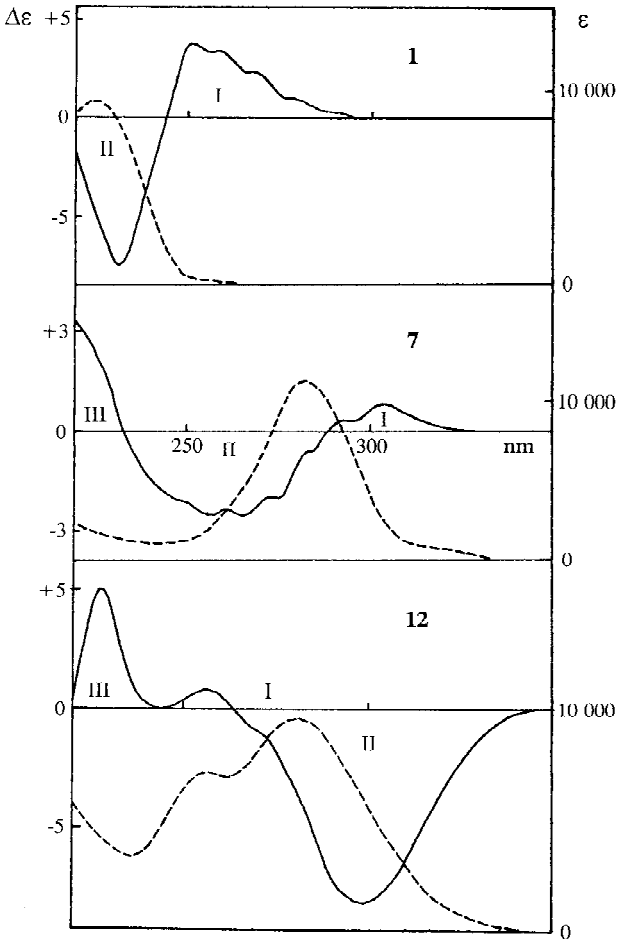



**Fig. 2.** CD (—) and UV (-----) spectra of **1, 7,** and **12** in heptane solution (in the range 220–350 nm). I: n − π* Cotton effect, II: π − π* Cotton effect, III short-wavelength Cotton effect.

band shows small, but recognizable, blue shift on changing solvent to more polar. For example enaminolactones **14, 17,** and **19** show $\lambda_{max}$ for this band at 200–203 nm in heptane solution, 199–200 nm in methanol, and 195–197 nm in hexafluoroisopropanol solution. The nature of this band remains obscure.

### *Molecular Structure of the Sulfur- and Nitrogen-Substituted 2(5H)-Furanones From X-Ray Diffraction*

The prerequisite for the application of the configurational rule for 2(*5H*)-furanones (Fig. 1) is the planarity of the 5-membered furanone ring. In order to ascertain the ring planarity in C(4)-heterosubstituted 2(*5H*)-furanones we have carried out an X-ray analysis for four representatives *i.e.,* **6, ent-11, 14,** and **17.** The molecules are illustrated in Figure 4[12] and selected bond lengths are listed in Table 8.*

In five cases investigated (**17** has two independent molecules in the asymmetric part of the unit cell) the furanone

*For numbering in this chapter see Figure 4.

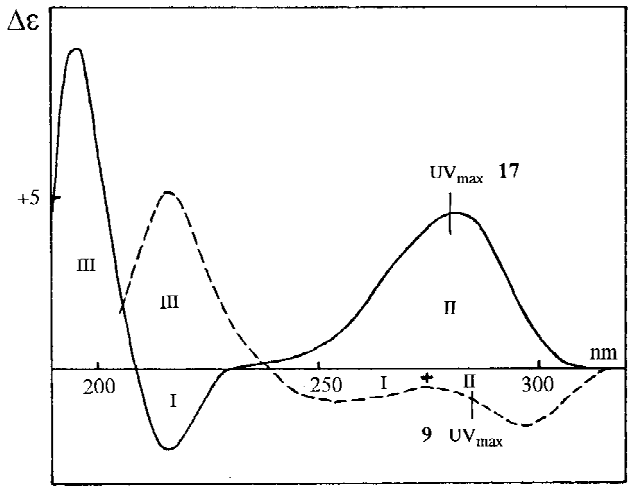



**Fig. 3.** CD spectra of **9** in methanol (-----) and **17** in hexafluoroisopropanol (—) solution. I: n − π* Cotton effect, II: π − π* Cotton effect, III: short-wavelength Cotton effect.

ring is almost planar with a maximum deviation of 0.024(2)Å for O(1) in **14.** At the same time N(1) is only 0.013(2)Å from this plane. Similarly, in both molecules of compound **17** nitrogen atom deviations from the furanone plane do not exceed deviations of atoms constituting the ring. This is one manifestation of the extensive conjugation of the N(1) lone pair, the C(3) = C(2) double bond and the C(1) carbonyl bond. The geometrical consequence of this conjugation is a significant shortening of the N(1)-C(3) bond to an average value of 1.331(7)Å, which might be compared with the average value of 1.355(14)Å for the C-N bond in C = C-N-$(C)_2$ system.[13] The shortening of the N(1)-C(3) bond is accompanied by the lengthening of the formally double C(3) = C(2) bond to an average value of 1.347(7)Å, as compared with the value of 1.323(13)Å quoted for cyclopentene and with 1.340(13)Å in conjugated systems.[13] The most striking geometrical change due to conjugation is seen in the furanone ring. Comparison with the non-fused furanones which contain oxygen function at C(4) (22 observations subtracted from the Cambridge Structural Database[14]) reveals significant shortening of the formally single C($sp^2$)- C($sp^2$) bond to an average value of 1.418(1)Å and simultaneous lengthening of the C(carbonyl)-O bond to a mean value of 1.382(10)Å. In non-fused furanones the two bonds have the mean values of 1.466(26)Å and 1.362(16)Å, respectively. This might indicate that the essential part of the electron delocalization is concentrated in the N(1), C(3), C(2), C(1), and O(2) region and takes place at the expense of delocalization within the ester function. The sum of the valence angles at the nitrogen atom is equal to 359.2° in **14,** and 359.8 and 359.0° in **17.** These values, as well as the deviations of nitrogen from the plane defined by its three substituents, [0.072(2), 0.028(2), 0.079(3)Å, for **14** and two molecules of **17,** respectively] indicate its $sp^2$ rather than $sp^3$ hybridization. Sulfur containing compounds **6** and **ent-11** also display a substantial amount of conju-

**TABLE 6. Substituent increments (nm) for the calculation of 2(*5H*)-furanone $UV_{max}$**

| Substituent | Solvent | |
|---|---|---|
| | Heptane | Methanol |
| Base value (no substituent) | 200 nm | 201 nm |
| Substituent at C-4 | | |
| Cl | +12 | +13 |
| Br | +20 | +21 |
| RO | [a] | +18 |
| HO | [a] | +22 |
| RS | +64 | +70 |
| RNH | +52 | +59 |
| $R_2N$ | +65 | +72[b] |
| Substituent at C-3 | | |
| Cl | +12 | +13 |
| Br | +18 | +19 |
| RO | [a] | +14 |
| HO | [a] | +26 |

[a]No data.
[b]Additional shift + 8 nm in hexafluoroisopropanol.

gation between sulfur and furanone moiety, although less pronounced than in compounds containing the nitrogen substituent. The average sulfur-furanone bond length of 1.716Å is somewhat shorter than the value of 1.751(17) quoted for this type of bond in the (C = C-S-C) system.[13] On the other hand, the C = C bond has the average length of 1.321(6)Å, comparable with the mean value observed in cyclopentene [1.323(13) Å] rather than in conjugated systems [1.347(7) Å].[13] In general, the geometry of the butenolide moiety closely resembles the average geometry of non-fused furanones and so it differs from the one observed in the nitrogen containing series. The C($sp^3$)-S and C(aryl)-S bond lengths have the values of 1.801(2) and 1.772(3)Å, respectively, typical for single bonds formed respectively by C($sp^3$) and C($sp^2$) carbon atoms with $sp^2$ hybrid of sulfur.[13]

### *2(5H)-Furanone Cotton Effects and Absolute Configuration*

The results of the X-ray structure investigations of several substituted 2(*5H*)-furanones presented above allow to conclude that the α,β-unsaturated lactone chromophore in heterosubstituted derivatives **B** can be treated as planar, as

**TABLE 7. Estimated shift (nm) of the CD n-π* band relative to the position of the π-π* band ($UV_{max}$)**

| Substituent at C-4 | Solvent | |
|---|---|---|
| | Heptane | Methanol |
| H | +50 | +40 |
| Br | +40 | +30 to +25 |
| Cl | +25 | +25 |
| RO | [a] | ca. 0 |
| RS | ca. 0 | −15 |
| RNH, $R_2N$ | −25 to −35 | −45 to −55[b] |

[a]No data.
[b]−63 nm in hexafluoroisopropanol.

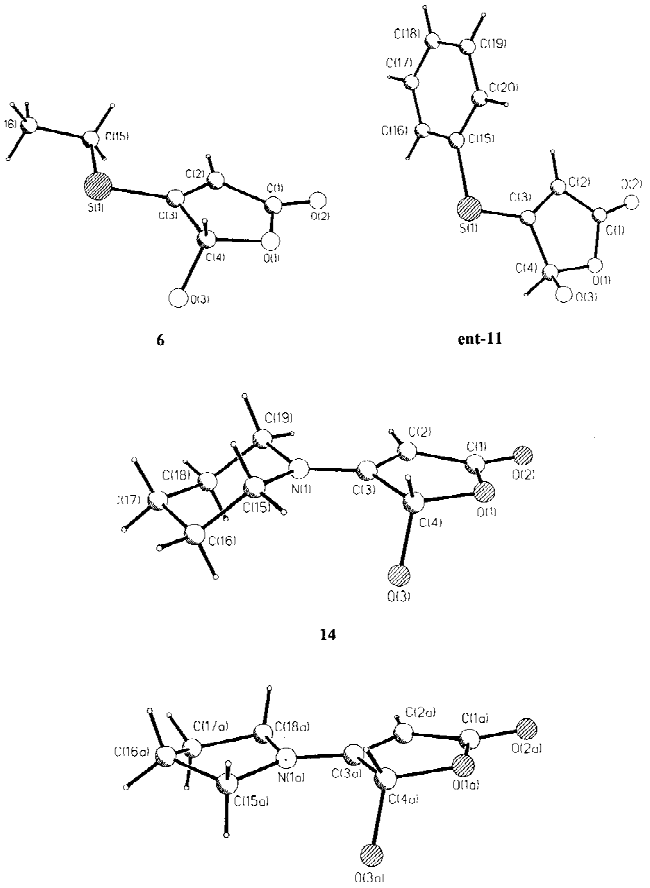



**Fig. 4.** Perspective view of furanones studied by X-ray diffraction and atom numbering scheme. Atoms belonging to menthyl substituent have been omitted for clarity.

it was the case with 2(*5H*)-furanones **A.** Thus the CD data in Tables 1–5 should be amenable to interpretation in terms of the 2(*5H*)-furanone configurational rule shown in Figure 1.

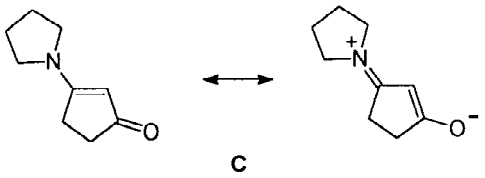
The halogen (**1–5**, Table 1), the mercapto (**6–13,** Table 2) and the hydroxy or alkoxy (**26–31,** Table 5) substituted 2(*5H*)-furanones obey the configurational rule with respect to the sign of either n − π* or π − π* Cotton effect. This is independent of the nature of the substituent at C(5), i.e., whether achiral or bearing centers of chirality, like the menthyl or bornyl groups.

The case of 4-amino substituted 2(*5H*)-furanones (Tables 3 and 4) is more complex. Whereas derivatives with the six-membered piperidinyl substituent **(14–16)** follow the configurational rule, those with the pyrrolidinyl **(17,18)** or the benzylamino **(20–22)** substituent or with two substituents at C(5) **(23–25)** display n − π* and π − π* Cotton effects of opposite sign to those predicted by the rule shown in Figure 1, assuming priority of the polar C-O bond over the C-C bond at C(5) in compounds **23–25.** The difference in the CD characteristics of closely structurally related enaminolactones, e.g., **14** and **17,** is striking (see also the "intermediate" case of 4-dimethylamino derivative **19**). While no comprehensive explanation of the differing behaviour of the 4-amino substituted 2(*5H*)-furanones can

**TABLE 8. Selected bond lengths (Å) in 2(*5H*)-furanones studied by X-ray diffraction[a]**

| Compound<br>Bond | **6** | **ent-11** | **14** | **17a** | **17b** |
|---|---|---|---|---|---|
| C(1)–C(2) | 1.457(4) | 1.442(5) | 1.419(3) | 1.419(8) | 1.416(8) |
| C(2)–C(3) | 1.327(3) | 1.315(5) | 1.351(3) | 1.338(8) | 1.353(8) |
| C(3)–C(4) | 1.508(3) | 1.508(5) | 1.514(3) | 1.489(7) | 1.511(6) |
| C(4)–O(1) | 1.442(3) | 1.434(5) | 1.442(2) | 1.434(5) | 1.434(7) |
| C(1)–O(1) | 1.357(3) | 1.370(4) | 1.373(3) | 1.378(7) | 1.396(7) |
| C(1)–O(2) | 1.199(3) | 1.195(4) | 1.217(3) | 1.212(8) | 1.211(9) |
| C(3)–N(1)[S(1)] | 1.716(3) | 1.715(4) | 1.335(3) | 1.336(7) | 1.321(7) |
| C(15)–N(1)[S(1)] | 1.801(3) | 1.772(4) | 1.468(3) | 1.463(8) | 1.459(7) |
| C(18)–N(1) | | | | 1.464(7) | 1.452(6) |
| C(19)–N(1) | | | 1.458(4) | | |

[a]Standard deviations are given in parentheses.




**C**

be esently offered, we would like to point to the known feature of enamines and enaminolactones bearing pyrrolidinyl substituent. The π-rotational barrier of enaminoketones of formula **C** is much higher than of analogs having either of the rings six-membered, the difference amounting to ca. 7.0 kcal/mol for both rings six-membered.[15]

It can be concluded that in substituted 2(*5H*)-furanones with low steric barrier to rotation of the 4-amino substituent the nature of the chromofore is different and the CD characteristics altered. This unexpected feature is now under study. However, chiroptical properties of other heterosubstituted 2(*5H*)-furanones are related to absolute configuration according to Figure 1. The configurational rule can be useful in determination of absolute configuration of 2(*5H*)-furanones of broad structural variety.

It is of interest to note that all the substituted 2(*5H*)-furanones collected in Tables 1–4 display positive Cotton effect III. While the origin of this Cotton effect is unknown, its consistent correlation of its sign with absolute configuration of the 2(*5H*)-furanone moiety is remarkable. In view of sensitivity of the Cotton effects of the n − π* and π − π* transitions of 4-amino substituted α,β-unsaturated lactones to the subtle structural changes, the sign of the short-wavelength Cotton effect III can be used as additional configurational indicator: positive for $R^1$-C-C = C bond system of M-helicity and negative for $R^1$-C-C = C bond system of P-helicity (cf. Fig. 1).

## EXPERIMENTAL PROCEDURES

### *Materials*

The synthesis of compounds used in this study has been reported: **5, 10, 13** (ref. 8), **3, 6, 14, 17, 19** (ref. 9), **23, 25** (ref. 10), **26** (ref. 16), **27** (ref. 17), **28** (ref. 11), **29** (ref. 18), **30** (ref. 19). Compound **31** was obtained by diazomethane methylation of the dihydroxy precursor.[20] The synthesis of other 2(*5H*)-furanones will be reported in due course.

**(*S*)- 4-Methoxy-5-methyl-2(*5H*)-furanone (27).** m.p. 30–32°C, $[\alpha]_D$ +27 (c = 0.5, MeOH); $^1$H NMR ($CDCl_3$, 300 MHz): δ 1.46 (d, 3H, J = 6.7 Hz), 3.89 (s, 3H), 4.83 (dq, 1H, J = 6.7, 0.9 Hz), 5.0 (d, 1H, J = 0.9 Hz); IR (KBr) 1750, 1610, 1210, 1180 $cm^{-1}$.

**(*R*)-3,4-Dimethoxy-5-hydroxymethyl-2(*5H*)-furanone (31).** oil, $[\alpha]_D$ −18 (c = 0.5, MeOH), $^1$H NMR ($CDCl_3$, 300 MHz): δ 1.97 (dd, 1H, J = 7.7, 6.4 Hz), 3.71–3.79 (m, 1H), 3.85 (s. 3H), 3.96–4.03 (m, 1H), 4.15 (s, 3H), 4.66 (dd, 1H, J = 4.2, 3.0 Hz), IR (neat) 3420, 2940, 1750, 1670, 1380 $cm^{-1}$.

### *Procedures*

The CD spectra were recorded with a Jobin-Yvon Dichrograph III and the UV spectra were obtained on a Shimadzu UV 160 spectrophotometer.

**X-ray data collection, solution, and refinement of the structures.** The reflection intensities were measured on a four-circle *KM*-4 (*KUMA Diffraction*) diffractometer with graphite monochromator. Cu Kα radiation was used for compounds **6, 14,** and **17** and Mo Kα radiation for compound **ent-11.** All measurements were performed at room temperature. The cell constants and the orientation matrix were obtained from a least-squares fit of at least 34 centered reflections. The reflections were measured using ω-2θ scan technique. Reflections for which [F > 4σ(F)] were considered as observed. The intensities were corrected for Lorentz and polarization effects, absorption corrections were not applied. The structures were solved by direct methods with SHELXS86[21] and refined with SHELX76[22] (**6, 7,** and **14**) and SHELXL93[23] (**ent-11**). Heavy atoms (C, O, N, S) were refined anisotropically. The positions of the H-atoms were calculated and refined using a riding model with a common isotropic temperature factor. Siemens Stereochemical Workstation was used to prepare drawings.[12] Details concerning the X-ray results will be published elsewhere.

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